HAUTE AUTORITÉ DE SANTÉ

PSYCHIATRY
New medicinal product
May 2017

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

INTUNIV (guanfacine), adrenergic alpha-agonist

No clinical benefit demonstrated in the management of severe attention-deficit hyperactivity disorder in children and adolescents aged 6 to 17 years in case of inefficacy, intolerance or contraindication to methylphenidate.

Main points

- INTUNIV is indicated for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents 6 to 17 years old for whom stimulants are not suitable, not tolerated or have been shown to be ineffective.
- Its quantity of effect is modest compared with the placebo on the symptoms of ADHD and remains uncertain in patients for whom methylphenidate is not suitable, was not tolerated and/or was not effective, given the lack of robust data in this sub-population.
- Due to a concerning safety profile with, in particular, short-term neuropsychiatric and cardiovascular adverse effects and unknown long-term adverse effects, ongoing monitoring for the occurrence of adverse effects such as somnolence, sedation, hypotension, bradycardia, weight gain and suicidal ideation must be carried out during titration, as well as during continuation of treatment.
- This is a last intention treatment.

Therapeutic strategy

- Management of ADHD is multimodal and combines several types of therapies depending on the patient. It comprises primarily psychological, educational and social measures which, if they really prove insufficient, can be combined, as second-line therapy, with a methylphenidate-based pharmacological treatment in children aged 6 years or older or adolescents. When a treatment with methylphenidate is prescribed, the global management strategy must be continued
- **Role of the proprietary medicinal product in the therapeutic strategy**
  INTUNIV can only be prescribed as a last intention treatment, only in case of ineffectiveness of a well-conducted treatment with methylphenidate in combination with psychological, educational and social measures, or intolerance or contraindication to methylphenidate.

Clinical data

- In five studies that enrolled children and adolescents with ADHD, treated or not with psychostimulants, the reduction in ADHD-RS-IV score (primary endpoint) was higher in the guanfacine groups regardless of dose, versus placebo, after 8 to 13 weeks of treatment, with an average reduction of 15 upto 26 points in the guanfacine groups, and of 6 up to 15 points in the placebo groups, for a total score of 54 points.
- In a 51-week study, after initial treatment of all patients with guanfacine, the failure rate (increase of ≥ 50% in the total ADHD-RS-IV score and ≥ 2 points in the CGI-S score) was lower in the group that continued with guanfacine than in the group switched to a placebo (49.3% versus 64.9% respectively, p=0.006).

- The adverse effects of guanfacine were orthostatic hypotension, bradycardia, somnolence, fatigue and headache. They are common. After stopping treatment, in particular after a sudden interruption, hypertensive rebound and tachycardia are events that may occur. The long-term effects on cognitive development are unknown.

Special prescribing conditions

- Medicinal product requiring special monitoring during treatment
- Initial three-month hospital prescription
- Prescription restricted to neurology, paediatrics and psychiatry specialists and departments

Benefit of the medicinal product

- The actual clinical benefit* of INTUNIV is low in the management of severe ADHD in children and adolescents aged 6 to 17 years in case of ineffectiveness of a well-conducted treatment with methylphenidate in combination with psychological, educational and social measures, or intolerance or contraindication to methylphenidate.
- INTUNIV does not provide any clinical added value** (CAV V) in the management of severe ADHD in children and adolescents aged 6 to 17 years in case of ineffectiveness of a well-conducted treatment with methylphenidate in combination with psychological, educational and social measures, or intolerance or contraindication to methylphenidate.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 17 May 2017 (CT-15974) and is available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the ACB, which can be substantial, moderate, low or insufficient for reimbursement of the medicinal product for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV (equivalent to “no CAV”) means “no clinical added value”.